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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/332,659	06/14/1999	FREDERIC ZENHAUSERN	4467-102US	3190

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EXAMINER

FORMAN, BETTY J

ART UNIT PAPER NUMBER

1634

DATE MAILED: 03/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/332,659

Applicant(s)

ZENHAUSERN, FREDERIC

Examiner

BJ Forman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-7,9,10,12-14,42 and 45 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1,4-7,9,10,12-14,42 and 45 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. <u>0304</u> . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>9/00,9/02</u> . | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> . |

Continuation of Attachment(s) 6). Other: Notice of Withdrawal from Issue.

DETAILED ACTION

1. Prosecution on the merits of this application is reopened on claims 1, 4-7, 9-10, 12-14, 42, 45 are considered unpatentable for the reasons indicated below:

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested:

METHOD FOR MONITORING A MOLECULAR SPECIES WITHIN A MEDIUM.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
4. Claims 1, 4-7, 9-10, 12-14, 42, 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
 - a. Claims 1, 4-7, 9-10, 12-14, 42, and 45 are indefinite in Claim 1 because the claim is drawn to a method for monitoring an enzymatic biomolecular reaction. However, the claim does not recite any methods steps of enzymatic reactions or biomolecular reactions. Therefore, it is unclear whether the method steps accomplish the claimed method.

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b. Claims 1, 4-7, 9-10, 12-14, 42, 45 are indefinite in Claim 1, line 5 for the recitation “reactingtag with the medium to attach to said nucleic acid reagent or product” because it is unclear whether the tag or some component of the medium is attached to the nucleic acid reagent or product. The recitation is further indefinite because the meets and bounds of nucleic acid reagent or product is unclear. The claimed reagent encompasses an enormous genus of reagents (e.g. buffers, nucleotides, various enzymes, labels, surfactants, intercalators and etc). Furthermore, the claimed nucleic acid product encompasses an extremely large genus of products (e.g. transcription products, translation products, replication products, degradation products, digestion products, ligation products, and etc.). As such, the meets and bounds of the claimed invention are indefinite.

c. Claims 13 and 14 are each indefinite for the recitation “the information detected” because the recitation lacks proper antecedent basis in Claim 1, which does not detect information. It is noted that Claim 1 recites “a nucleic acid is detectable by the multisensor to provide information”. However, this recitation merely defines the nucleic acid as being detectable. The recitation does not provide the method with a detection step. Furthermore, the recitation does not provide antecedent basis for “the information detected” recited in the dependent claims. It is suggested that the claims be amended to provide proper antecedent basis.

d. Claim 45 is indefinite for the recitation “further comprising the step of controlling” because it is unclear where within the method steps of Claim 1 the additional step is performed.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 7, 9-10, 12-14, 42 are rejected under 35 U.S.C. 102(e) as being anticipated by Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997).

Regarding Claim 1, Van Ness et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product (fragment) (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information “representative” of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33). The instant specification broadly defines the “multisensor array” at pages 21-23 as being at least two different sensors (page 21, line 20). Van Ness et al teach numerous sensors including embodiments wherein the multisensor array comprises multiple mass spectrometer detectors (Column 64, lines 44-47) of a quadrupole mass analyzer (Column 59, lines 1-22 and Column 67, lines 6-10). Hence, Van Ness et al teach the multisensor array as claimed.

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Regarding Claim 7, Van Ness et al disclose the method wherein the multisensor array comprises at least one of a vibrating (Column 57, line 65-Column 58, line 8) or resonant micromechanical device (Column 60, lines 2-23).

Regarding Claim 9, Van Ness et al disclose the method wherein the multisensor array comprises a mass spectrometer (Column 59, lines 1-22).

Regarding Claim 10, Van Ness et al disclose the method wherein the multisensor array comprises an optical sensing probe (Column 63, lines 50-57).

Regarding Claim 12, Van Ness et al disclose the method wherein the information comprises volatile chemical species characteristic of the presence of the nucleic acid (Column 67, lines 1-28).

Regarding Claim 13, Van Ness et al disclose the method wherein the information includes a change in the concentration of nucleic acids i.e. cleavage of the tag from the nucleic acid (Column 63, lines 1-50).

Regarding Claim 14, Van Ness et al disclose the method wherein the information includes the a change in at least one secondary product of the reaction i.e. cleavage of the tag (Column 63, lines 12-23).

Regarding Claim 42, Van Ness et al disclose the method wherein the reaction is PCR (e.g. Column 18, lines 21-29 and Column 65, lines 64-67).

7. Claims 1, 7, 9, 12-14, 42 and 45 are rejected under 35 U.S.C. 102(3) as being anticipated by Koster et al (U.S. Patent Application Publication No. 2002/0009394, filed 2 April 1999).

Regarding Claim 1, Koster et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product, screening the medium with a multisensor array (§ 81) whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable to provide information to produce a signal output, transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means, sorting the information in accordance with a set of class boundaries and monitoring the information "representative" of the identity and amount of nucleic acid (§ 108-125).

Regarding Claim 7, Koster et al disclose the method wherein the multisensor array comprises a resonant micromechanical device (i.e. FTICR, § 81).

Regarding Claim 9, Koster et al disclose the method wherein the multisensor array comprises a mass spectrometer (§ 81).

Regarding Claim 12, Koster et al disclose the method wherein the information comprises volatile chemical species characteristic of the presence of the nucleic acid (§ 132-133).

Regarding Claim 13, Koster et al disclose the method wherein the information includes a change in the concentration of nucleic acids e.g. expression which determines concentration in the cell (e.g. § 5) or following PCR which determines changes of concentration i.e. amplification (§ 86).

Regarding Claim 14, Koster et al disclose the method wherein the information includes the a change in at least one secondary product of the reaction i.e. ionization (§ 110-119)

Regarding Claim 42, Koster et al disclose the method wherein the reaction is PCR (e.g. § 86).

Regarding Claim 45, Koster et al disclose the method further comprising controlling the PCR reaction i.e. computer controlled thermocycler (§ 94-97).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997) in view of Freidhoff et al (U.S. Patent No. 5,386,115, issued 31 January 1995).

Regarding Claims 4-6, Van Ness et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product (fragment) (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, Column 67, lines 1-19), transferring the signal to a signal processing means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information "representative" of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33).

Van Ness et al further teach the method wherein the sensor comprises anyone of many known in the art (e.g. Column 64, line 48-Column 65, line 19) but they do not specifically teach the sensor comprises a semiconductor gas sensor (Claim 4); a metal oxide gas sensor (Claim 5); or a conductive polymer sensor (Claim 7). However, the claimed sensors were well known in the art at the time the claimed invention was made as taught by Freidhoff et al who

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teach their multisensor array (Fig. 1) comprising a semiconductor gas sensor (Column 3, lines 47-57) comprising a metal oxide gas sensor (Column 5, lines 39-54) and comprising a conductive polymer sensor (i.e. electrodes of conductive material, Column 5, lines 7-17).

Freidhoff et al teach their semiconductor gas sensor is small, low power, easily transportable and has the ability to detect multiple constituents simultaneously thereby providing a low cost sensor having wide applications (Column 2, lines 25-30).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sensor of Freidhoff et al to the gas sensor in the method of Van Ness et al based on the preferred teaching and advantages taught by Friedhoff et al. Specifically, one of ordinary skill would have been motivated to use the small, low power, easily transportable sensor of Friedhoff et al for the expected benefits of providing a low cost sensor having wide applications (Column 2, lines 25-30).

10. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness et al (U.S. Patent No. 6,312,893, filed 22 July 1997) in view of Koster et al (U.S. Patent Application Publication No. 2002/0009394, filed 2 April 1999).

Regarding Claim 45, Van Ness et al disclose a method for monitoring a reaction comprising the steps of reacting one or more volatile organic tags with a medium to attach the tag to a nucleic acid product (fragment) (Column 8, lines 18-65), screening the medium with a multisensor array whereby more than one physico-chemical change of a gas or vapor phase of a nucleic acid is detectable (Column 57, line 38-Column 65, line 19) to provide information to produce a signal output, Column 67, lines 1-19), transferring the signal to a signal processing

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means for generating a final output, receiving the final output into a pattern recognition means (software program), sorting the information in accordance with a set of class boundaries (analyzer) and monitoring the information "representative" of the identity and amount of nucleic acid (Column 67, lines 20-28 and Claims 1-33).

Van Ness et al teach the method wherein the reaction is PCR (e.g. Column 18, lines 21-29 and Column 65, lines 64-67) but they do not specifically teach controlling the PCR. However, it was well known in the art at the time the claimed invention was made that PCR is routinely performed by repeated cycles of high and low temperatures controlled by a thermocycler (see Koster et al: ¶ 94-97). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to control the PCR in the method of Van Ness et al based on the well known use of thermocyclers for PCR as taught by Koster et al (¶ 94-97) for the obvious benefit of using routinely practiced methods to thereby obtain desired results i.e. amplification.

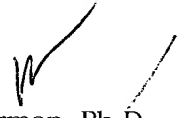
Conclusion

11. No claim is allowed.
12. The examiner for this application has changed. Please address future correspondence to BJ Forman, Art Unit: 1634.
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:00 TO 3:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
March 4, 2004

